

Appln. No. 10/069,282

Amd. dated April 30, 2004

Reply to Office Action of January 30, 2004

REMARKS

Claims 1-5 and 8-27 currently appear in this application. The Office Action of January 30, 2004, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Election/Restriction

Applicant hereby confirms the election with traverse the species of example 3, compound of Group II, claims 1-3, 5-21 and 23-27. It is respectfully submitted that all of the claimed compounds have the same activity, namely, they act as antagonists against but not as agonists for the androgen receptor. All of the claimed compounds are androstane derivatives having substituents in the 7- or 11-position.

Specification

The abstract of the disclosure is objected to because of its length. Accordingly, a new abstract of the disclosure is submitted herewith on a separate sheet.

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Additionally, the specification has been amended to correct self-evident typographical and syntactical errors. No new matter has been added.

Rejections under 35 U.S.C. 112

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is respectfully traversed. Claim 5 has been amended to recite "wherein Ar, A and R1 have the same meanings as defined in claim 1."

Art Rejections

Claims 1, 2, 5-7, 11-13, 18, 19 and 24-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Grunwell et al.

This rejection is respectfully traversed. Grunwell et al. teach, at column 3, lines 58-60 and column 8, line 58 to column 9, line 46, the following:

The isomerization from 3-keto-7( $\alpha,\beta$ -loweralkyl)- $\Delta^5$ -steroids to the corresponding  $-\Delta^4$ -steroids takes place with great facility. The androstane derivatives having an

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isopropyl group in the 7-position are disclosed in Example XII at column 19, lines 30-54. The 4-ene androstane derivatives have some biological properties, including anabolic, androgenic and estrogenic and other hormonal properties. Moreover, the 4-ene androstane derivatives are said to be useful in treating prostatic hypertrophy (column 3, lines 58-70 and column 9, line 75 to column 10, line 16).

The 5-ene-androstane derivatives have some biological properties such as anabolic, androgenic, Claudogenic, pregestation, and anti-progestational activities, as disclosed in column 1, lines 14-16 and column 9, lines 62-75). In addition, the 5-ene-androstane derivatives are useful as anti-fertility agents (column 9, lines 50-55) and exhibit both progestational and anti-progestational activity (column 9, lines 57-61).

As is clear from the above, Grunwell et al. neither disclose nor suggest that 4-ene-androstane derivatives of 5-ene-androstane derivatives are useful as anti-androgenic agents and pure antagonists. In addition, as pointed out above, the compounds of Grunwell et al. exhibit an androgenic property, namely, an agonistic action. Furthermore, some of the 5-ene-androstane derivatives have both progestational and anti-progestational activity, namely, both agonistic and antagonistic action. It is clear from the properties of the

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Grunwell et al. compounds that they are not the same as the compounds herein claimed, nor do they suggest any of the compounds claimed herein.

Claim 1 has been amended to delete the language "and the dashed line in combination with the solid line represents the formation of a single bond or a double bond", as well as substituting a formula without the dashed lines for the general formula. Since the dashed line has been deleted from the general formula (I), claim 6 is cancelled. Since X1 is limited to a hydrogen atom, claim 7 is no longer necessary and, accordingly, claim 7 has been cancelled.

It is respectfully submitted that the compounds now claimed do not overlap those of Grunwell et al.

Claims 1, 2, 5, 7, 8, 11-13, 18, 19, 21 and 24-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Pierdet et al.

This rejection is respectfully traversed. Claim 1 has been amended to delete the language "and the dashed line in combination with the solid line represents the formation of a single bond or a double bond", as well as substituting a formula without the dashed lines for the general formula. It is respectfully submitted that the compounds now claimed do not overlap those of Pierdet et al.

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There is nothing in Pierdet et al. that suggests that the generic group of compounds disclosed therein act as a pure antagonist or show an anti-androgenic activity. Pierdet et al. only teach novel haptens and antigens of Formula I, such as  $7\alpha$  and  $7\beta$ -( $\omega$ -carboxydecyl)- $\Delta$ -androstene-17 $\beta$ -ol-3-one.

In other words, the compounds of Pierdet et al. act as an antigen after binding to bovine serum albumin (BSA), as disclosed in column 10, lines 13-26. Moreover, it is inferred from column 14, example 7, that the substituents in the 7- and 11-positions play a role in forming a covalent bond with BSA by using the extreme carboxyl group of the substituents. This is not true for the compounds claimed herein.

Claims 1, 2, 5-8, 11-13, 18, 19 and 24-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Labrie et al.

This rejection is respectfully traversed. Claim 1 has been amended to disclaim the Labrie et al. compounds.

Claims 1, 2, 5, 7, 8, 11-13, 18, 19 and 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grunwell et al.

This rejection is respectfully traversed. Claim 1 has been amended to delete the language "and the dashed line in combination with the solid line represents the formation of

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a single bond or a double bond", as well as substituting a formula without the dashed lines for the general formula.

It is respectfully submitted that there is nothing in Grunwell et al. that suggests the compounds of the present invention. Additionally, the compounds in Grunwell et al. do not have the same activities as the compounds claimed herein, namely, the claimed compounds act as antagonists against but not as agonists for the androgen receptor.

Claims 1, 2, 5, 7, 8, 11-13, 18, 19, 21 and 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pierdet et al.

There is nothing in Pierdet et al. that suggests the compounds of the present invention, which compounds act as antagonists but not as agonists for the androgen receptor. The Pierdet et al. compounds are used for preparing antigens.

As noted above, neither Grunwell et al. nor Pierdet et al. provide any teachings or suggestions that would lead to compounds having anti-androgenic activity and which act as a pure antagonist. In fact, Grunwell et al. disclose compounds having properties which are opposite to those of the present invention. Although Grunwell and Pierdet et al. disclose unsaturated ketones containing 4-ene or 5-ene, they do not at all teach the saturated ketones as claimed herein.

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Therefore, it is respectfully submitted that it would not have been obvious to one having ordinary skill in the art at the time the present invention was made to conceive of the compounds of the present invention based on the teachings of Grunwell et al. or Pierdet et al. The compounds in the cited references differ from the compounds claimed herein in terms of the scaffold of the compounds and the uses thereof.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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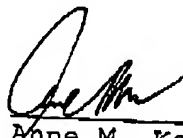
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In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

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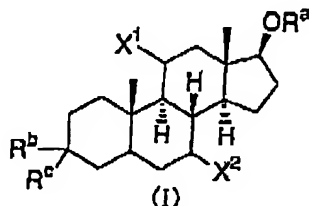
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## ABSTRACT OF THE DISCLOSURE

Compounds represented by general formula (I),  
pharmaceutically acceptable salts thereof, or prodrugs of the  
compounds or their salts:



Wherein X1 is a hydrogen atom, X2 is, for example a  
carboxyheptyl group, Ra is, for example, hydrogen, Rb and Rc  
for example, taken together with the carbon atom in the 3-  
position to which they are bound represent an optionally  
protected  $-(C=O)-$ , are useful as antiandrogenic agents and can  
be used as preventives or therapeutics of diseases such as  
prostate cancer, prostatomegaly, male pattern alopecia, sexual  
prematurity, acne vulgaris, seborrhea, and hirsutism